Application of a low cost array-based technique - TAB-Array - for quantifying and mapping both 5mC and 5hmC at single base resolution in human pluripotent stem cells.

Journal: Genomics

Publication Year: 2014

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PubMed link: 25179373

Funding Grants: TSRI Center for hESC Research, The Stem Cell Matrix: a map of the molecular pathways that define pluripotent cells, Ensuring the safety of cell therapy: a quality control pipeline for cell purification and validation, Collaborative Laboratory for Human Embryonic Stem Cell Research at Sanford-Burnham Medical Research Institute

Public Summary:
We have developed a method for mapping 5-hydroxymethylcytosine (5hmC) in human pluripotent stem cells and their derivatives. We find that 5hmC profiling reveals far more about epigenetic changes during differentiation of human pluripotent stem cells than conventional 5-methylcytosine profiling.

Scientific Abstract:
5-hydroxymethylcytosine (5hmC), an oxidized derivative of 5-methylcytosine (5mC), has been implicated as an important epigenetic regulator of mammalian development. Current procedures use DNA sequencing methods to discriminate 5hmC from 5mC, limiting their accessibility to the scientific community. Here we report a method that combines TET-assisted bisulfite conversion with Illumina 450K DNA methylation arrays for a low-cost high-throughput approach that distinguishes 5hmC and 5mC signals at base resolution. Implementing this approach, termed "TAB-array", we assessed DNA methylation dynamics in the differentiation of human pluripotent stem cells into cardiovascular progenitors and neural precursor cells. With the ability to discriminate 5mC and 5hmC, we identified a large number of novel dynamically methylated genomic regions that are implicated in the development of these lineages. The increased resolution and accuracy afforded by this approach provides a powerful means to investigate the distinct contributions of 5mC and 5hmC in human development and disease.